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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,726	01/26/2006	Amanda Proudfoot	ARS-106	6045

23557 7590 07/25/2008

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
07/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,726	PROUDFOOT ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I and the antagonist of mutants of CXCL11 in the reply filed on 4/30/2008 is acknowledged. The traversal is on the ground(s) that the instant application is a national stage application and is subject to the unity of invention rules for restriction. The previous requirement for restriction was deemed appropriate in view of the polypeptide disclosed by NCBI Accession No. Q9JHH5. However, the Applicants argue that newly submitted claims 52-75 share at least one special technical feature not disclosed by the polypeptide of NCBI Q9JHH5, and thus request reconsideration of the restriction requirement.

These arguments have been fully considered and are found persuasive because the polypeptide of NCBI Accession No. Q9JHH5 does not contain a substitution, or pattern of substitutions, as recited in the pending claims.

2. Claims 52-75 are currently pending and are the subject of this office action.

Information Disclosure Statement

The information disclosure statement received on 6/30/2006 has been fully considered.

Claim Objections

1. The Examiner suggests amending claim 1, part (g) to recite "are substituted with Alanine or Glycine".

2. The Examiner suggests amending claim 61 to remove the “or” at the end of the claim.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the CXCL11 antagonists represented by the polypeptide sequences of SEQ ID NOs 3-5, does not reasonably provide enablement for any other isolated antagonists of CXCL11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims of the instant invention are drawn to an isolated polypeptide antagonist of CXCR-3-binding CXC chemokines, wherein said antagonist comprises a mutant of CXCL11. The claims recite mutant CXCL11 polypeptides having substitutions in at least one of several basic residues numbered on the sequence of human mature CXCL11, including residues 46, 62, or 70. The claims further recite mutant CXCL11 polypeptides comprising a substitution in at least one of these residues, and further substitution at various other amino acid positions, including positions 49, 52, 57, 59, 66, and 71, the first nine amino acids of mature CXCL11, and various combinations thereof. The claims also recite pharmaceutical compositions comprising the claimed isolated antagonist, nucleic acids and vectors encoding said antagonist, and isolated host cells comprising said antagonist polypeptide.

The isolated polypeptide antagonists of independent claim 52 can comprise a substitution in at least one of residues 46, 62, or 70, wherein said substitution comprises numerous recited amino acids substituted at these positions. The specification provides guidance and examples showing the that the polypeptides of SEQ ID NO: 3-5 are mutant CXCL11 polypeptides capable of binding the CXCR3 receptor but exhibiting reduced heparin binding, and further capable of antagonizing cell recruitment in response to wild-type CXCL11. However, there is no guidance or example showing any other mutant CXCL11 polypeptide is capable of functioning as an antagonist of CXCL11. The isolated polypeptide antagonists of independent claim 52 can comprise a substitution in at least one of residues 46, 62, or 70, wherein said substitution comprises numerous recited amino acids substituted at these positions. Although the specification provides guidance and examples of mutant CXCL11 polypeptides comprising

substitutions at positions 46, 62, and 70, and additional substitutions at positions 49, 52, 57, 59, 66, and/or 71, the language of the claims, reciting substitution in "at least one" of these residues, does not limit the substitutions to only these residues. As written, the claims only have to have “at least” one substitution at position 46, 62, 66, or 70, and can therefore also comprise a substitution at any other position within the polypeptide. The specification does not provide guidance and examples showing which amino acid at any position, other than the positions mutated in SEQ ID NOs 3-5, can be substituted and still result in a polypeptide that can function as an antagonist of CXCL11. Furthermore, part (j) of independent claim 52, as well as dependent claim 66, recites isolated mutant polypeptide antagonists of CXCL11 comprising the substitutions discussed above, and also further comprising mutation in one or more amino acids residues in order to decrease the aggregation properties of the claimed CXCL11 antagonists. As written, claim 52(j) and claim 66 read on virtually unlimited mutation within any CXCL11 antagonist; however, the specification does not provide guidance or examples which teach which amino acids can be mutated in order to achieve this effect, or which amino acid residues must be conserved.

It is also noted that independent claim 52 and its dependent claims recite substitution with various amino acid residues. Although the specification provides guidance and examples showing substitution of various amino acid residues with alanine, there are no examples showing substitution with any other amino acid. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein’s function. As an example of the unpredictable effects of mutations on protein function, Mickle *et al* (Med. Clin. North Am., 2000, Vol. 84(3), p. 597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR – p. 597). Several mutations can cause cystic fibrosis, including the G551D mutation. In this mutation, a glycine replaces the aspartic acid at position 551, giving rise to the cystic fibrosis phenotype. In the most common cystic fibrosis mutation, Δ-F508, a single phenylalanine is deleted at position 508, giving rise to the cystic fibrosis phenotype. Thus, even the substitution or deletion of a single amino acid can have dramatic and *unpredictable* effects on the function of the protein. Although the teachings of Mickle are in relation to CFTR rather than CXCL11, Mickle nevertheless illustrates the inherent unpredictability regarding the effects of mutation on the biological activities and properties of a given polypeptide. Therefore, one of ordinary skill in the art would not be able to predict, which further, undue experimentation, which additional amino acid residues of CXCL11 can be substituted, and which amino acids other than alanine could be substituted, in order to maintain the ability of a mutant polypeptide to function as a CXCL11 antagonist.

In summary, the breadth of the claims is excessive because the claims read on mutant CXCL11 polypeptides comprising substitutions in the recited residues, but also potentially in any other residue within the CXCL11 polypeptide. The specification provides guidance showing only the polypeptides of SEQ ID NOs 3-5, but does not provide guidance or examples of any other polypeptide that can function as a CXCL11 antagonist, or teach which additional residues can be substituted and still retain antagonist function. Finally, due to the unpredictability inherent in mutating amino acids within a given protein, a person of ordinary skill in the art would not predict how to make and use any CXCL11 antagonist other than those of SEQ ID NOs 3-5 without further, undue experimentation.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647